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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,677	09/14/2001	Christine Libon	PF95PCTSEQ/D	9128

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EXAMINER	
NAVARRO, ALBERT MARK	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,677	LIBON ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-58 and 60-64* is/are pending in the application.

4a) Of the above claim(s) *29-44,52-55,60 and 61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-51,56-58 and 62-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment filed January 14, 2005 has been received and entered. Consequently claims 29-58 and 60-64 are pending in the instant application, of which claims 29-44, 52-55, and 60-61 have been withdrawn from further consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

1. The rejection of claims 50-51 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of stimulating an immune response, does not reasonably provide enablement for methods of preventing cancer is withdrawn in view of Applicants amendments.

2. The rejection of claims 45-51, 56-58, and 62-64 under 35 U.S.C. 112, second paragraph, as being vague and indefinite in the recitation of "in need thereof" is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. The rejection of claims 56-58, and 63-64 under 35 U.S.C. 102(b) as being anticipated by d'Hinterland et al is withdrawn in view of Applicants amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The rejection of claims 45-49, and 62 under 35 U.S.C. 103(a) as being unpatentable over d'Hinterland et al in view of Henderson and Teicher et al is maintained. Additionally, in view of Applicants amendments this rejection is applied to claims 50-51, 56-58, and 63-64.

Applicants are asserting that the Office fails to note that tumor destruction as disclosed in Henderson is facilitated by the heterologous expression of a highly visible antigen which specifically elicits NK cells to the tumor cells. Applicants assert that the Office has referenced the prior art teaching of a DNA-mediated tumor vaccine which genetically modifies cells to become more immunogenic to elicit NK cells (Column 14, line 45), such methods being absent with the instant method of inducing an antitumor immune response. Applicants conclude that one skilled in the art would not conclude from the teaching of Henderson that NK cells would be elicited to a tumor which does not express the highly visible antigen to elicit NK cells as disclosed.

Applicants arguments have been fully considered but are not found to be fully persuasive.

First, Applicants assert that the Office fails to note that tumor destruction as disclosed in Henderson is facilitated by the heterologous expression of a highly visible antigen which specifically elicits NK cells to the tumor cells. However, Applicants are respectfully directed back to their own claim language which recite methods of stimulation/compositions which "comprise" proteoglycans and an anticancer treatment. The presence of additional teaching above and beyond that claimed by Applicants is expressly permitted by the use of this transitional phrase. Accordingly, a method of stimulating an immune response which is facilitated by the heterologous expression of a highly visible antigen does not detract from the art teaching each and every limitation of the instantly filed claims.

Second, Applicants assert that the Office has referenced the prior art teaching of a DNA-mediated tumor vaccine which genetically modifies cells to become more immunogenic to elicit NK cells (Column 14, line 45), such methods being absent with the instant method of inducing an antitumor immune response. However, as set forth directly above, this additional teaching, which may be absent from the instantly filed application, is simply not excluded from being present, based upon the transitional phrase employed of "comprising."

Finally, Applicants conclude that one skilled in the art would not conclude from the teaching of Henderson that NK cells would be elicited to a tumor which does not express the highly visible antigen to elicit NK cells as disclosed. However, this teaching

simply cannot be excluded in the first place, since the claims allow for performing exactly that, expressing a highly visible antigen to elicit NK cells. Furthermore, dictionary.com defines NK cells as "a large granular lymphocyte capable of killing a tumor or microbial cell ***without prior exposure to the target cell*** and without having it presented with or marked by a histocompatibility antigen." (Emphasis added). In other words, those of ordinary skill in the art recognize that NK cells are naturally elicited against tumor cells. Given that NK cells are naturally elicited against tumor cells, it would have been prima facie obvious to have combined a membrane fraction, comprising proteoglycans to stimulate these natural killer cells which are known to attack tumor cells. It would have been further obvious to have combined this with anti-cancer treatments, since both NK cells and anticancer treatments work in the same manner to destroy tumor cells.

The claims are drawn to a method of stimulating an immune response and/or inducing an antitumor immune response in a mammal, including a human, in need thereof whereby a membrane fraction of Gram negative bacteria, comprising proteoglycans is administered in the form of a pharmaceutical composition in combination with an anticancer treatment in an amount effective to result in such induction and or stimulation.

d'Hinterland et al (US Patent Number 4,501,693) teach of isolated membranous proteoglycan from K. pneumoniae which activates sharply the stimulation of NK cells. (See column 1).

d'Hinterland et al do not teach of anticancer treatments.

Henderson (US Patent Number 5,648,478) teach of tumor vaccines which elicit NK cells to destroy tumor cells. (See column 14).

Teicher et al (US Patent Number 5,776,898) teach of standard treatments for tumors, including antiangiogenic agents, and chemotherapy. (See column 7).

Given that 1) d'Hinterland has taught that membranous proteoglycan isolated from *K. pneumoniae* stimulates NK cells, and that 2) Henderson et al has taught of tumor vaccines which elicit NK cells to destroy tumor cells, and that 3) Teicher et al have taught of standard modalities for treating cancer, including antiangiogenic agents and chemotherapy, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have incorporated the composition of membranous proteoglycan isolated from *K. pneumoniae* as taught by d'Hinterland et al and combined the composition with the tumor vaccine taught by Henderson. It would have been further obvious to combine standard cancer treatment such as chemotherapy as taught by Teicher since they both result in the same end effect, a destruction or slowing the growth of a tumor. One would have been motivated to combine the tumor vaccine and the proteoglycans isolated from *K. pneumoniae* in view of the shared mechanism of action, the stimulation of NK cells.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Navarro
Primary Examiner
March 8, 2005

MARK NAVARRO
PRIMARY EXAMINER